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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/871,212	05/31/2001	Suresh K. Tikoo	293102003000	1691

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EXAMINER	
WINKLER, ULRIKE	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 08/27/2003

21

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/871,212	TIKOO ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *June 10, 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6,9-17,21,22,27,28,35,41-43 and 46-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/7/02 & 6/10/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Amendment filed June 10, 2003 (Paper No. 20) in response to the Office Action of December 10, 2002 is acknowledged and has been entered. Claims 1, 2, 8-17, 21, 22, 25, 27, 28, 35, 41-43, 46-51 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Drawings

The office acknowledges the receipt of the new Figure 8. The drawings have been reviewed and approved by the Draftsperson.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 16, is attached to the instant Office action.

Claim Rejections - 35 USC § 112

The rejection of claims 1, 2, 12, 13, 14, 21, 22, 25, 27, 28, 35, 43, 50, 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for changing the viral tropism of a bovine adenovirus to infect a human cell line by substituting the human adenovirus fiber protein, does not reasonably provide enablement for altering the viral tropism by changing only the hexon or penton protein **is withdrawn** in view of applicants declaration and citation of Vigne et al (Journal of Virology, 1999).

Applicants further would like to have clarification whether the restriction requirement is being withdrawn in view of the enablement rejection. For clarification the restriction requirement is maintained regardless of the enablement rejection. Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the specification or the restriction requirement are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In other words just because applicants have elected the fiber protein for prosecution this limitation is not read into all claims and the claims are not limited to fiber unless specifically stated.

The declaration filed under 37 CFR 1.132 filed Suresh K. Tikoo is sufficient to overcome the rejection. The claims are drawn to changing fiber protein or pIX protein, the declaration shows pBAV950 comprising a modified capsid gene was able to infect human cells (HeLa and A549), while BAV600 which a bovine adenovirus comprising the human fiber protein alone was shown to be able to infect not only human cells but a variety of other non-bovine cells. The ability to infect a variety of unrelated cells was an unexpected result. Note the declaration makes references to prior art that has not been listed on a 1449 form and therefore has not been fully considered.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 2, 5, 6, 9-11, 14-17, 21, 22, 27, 28, 35, 41, 42, 43, 46-49 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mittal et al. (U.S. Pat. No. 5,820,868, 1998, see IDS Paper No. 3), Krasnykh et al. (Journal of Virology, 1996, see IDS

Paper No. 3) and Reddy et al. (Journal of Virology, 1999, see IDS Paper No. 3) **is maintained** for reason of record.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In order to find predictability it is necessary to have some indication that the BAV is similar to the HAd sequences and organization and that altering the fiber construct would alter the ability of the virus to infect different cells.

In this case, Mittal et al. disclose the production of a recombinant bovine adenovirus for the production of foreign proteins, which are immunogenic and can function as a vaccine (see column 1,lines 28-33; column 13, lines 18-20; column 13, line 65 to column 14, line 10). The reference discloses a recombinant vector system comprising the entire BAV DNA and a plasmid or virus by *in vivo* recombination following cotransfection of a suitable cell line (column 4, lines 48-55). The reference also teaches the cloning and sequencing of the BAV E3 region and the fiber genes (see example 3). The general organization of adenovirus genomes seems to be well conserved; therefore, the regions of sequences could be predicted from the human adenovirus genome map. The fiber protein is present on the surface of the virion and is involved in a number of functions including attachment of the virus to the cell surface during infection, assembly of virion and antigenicity (column 23, lines 49-53).

Krasnykh et al. teach the modification and alteration of the adenoviral fiber protein in order to alter the viral tropism. The modification of the fiber protein alters the receptor recognition profile of the virus (see abstract) allowing for the attachment to a non-permissive cells.

Reddy et al. provides the motivation to use BAV-3 as a viral vector for therapy in humans. For successful therapy, transfer vectors with very high transudation efficiency are needed. A strategy to achieve this is to replace the knob region of the fiber of BAV-3 with that of an HAV. This is possible, as the entry of ovine adenovirus into human cells was enhanced when the knob region of the fiber was replaced with that of HAV-5 (see page 9143, last paragraph).

Therefore, taken as a whole Reddy et al suggest using BAV-3 vector for therapy by replacing the fiber protein. One having ordinary skill in the art would have been motivated to utilize the bovine adenovirus as a vaccine vector because the average human population would not have produced neutralizing antibodies to bovine adenovirus as this virus would not normally infect the population. Utilizing a bovine adenovirus as a vaccine vector would also reduce the risk of recombination with wild type viral sequences creating a replication competent virus. Therefore, the instant invention is obvious over Mittal et al., Krasnykh et al. and Reddy et al.

The rejection of claims 1, 2, 5, 6, 9-17, 21, 22, 27, 28, 35, 41, 42, 43, 46-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Romanczuk et al. (WO 99/36545, see IDS Paper No. 3) and Reddy et al. (Journal of Virology, 1999, see IDS Paper No. 3) **is maintained** for reasons of record.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, Romanczuk et al. teaches the production of chimeric adenovirus vector by modifying the capsid protein with a heterologous ligand to improve or alter the infectious capability of the vector. The vectors can be used to deliver a transgene into a cell (see abstract, claims 1, 2, 18 and 43). The reference is not limited to a this particular adenovirus as any adenovirus falls within the scope of the invention.

Reddy et al. provides the motivation to use BAV-3 as a viral vector for therapy in humans. For successful therapy, transfer vectors with very high transudation efficiency are needed. A strategy to achieve this is to replace the knob region of the fiber of BAV-3 with that of an HAV. This is possible, as the entry of ovine adenovirus into human cells was enhanced when the knob region of the fiber was replaced with that of HAV-5 (see page 9143, last paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a bovine adenovirus for the transuduction of human cell lines or for the use of the bovine adenovirus as a vaccine vector. Reddy et alprovides the motivation to produce a bovine adenovirus with altered tropism to infect human cells. Romanczuk et al. teaches a generic chimeric adenoviral vector to alter tropism. One having ordinary skill in the art would have been

motivated to utilize a bovine adenovirus as a vaccine vector because the average human population would not have produced neutralizing antibodies to bovine adenovirus as this virus would not normally infect the population. Utilizing a bovine adenovirus as a vaccine vector would also reduce the risk of recombination with wild type viral sequences creating a replication competent virus. Additionally utilizing BAV type 1 and 2 would allow for multiple vaccination with a bovine adenovirus vector as the subject would not have made neutralizing antibodies to the particular vectors. Therefore, the instant invention is obvious over Romanczuk et al. and Reddy et al.

Conclusion

No claims allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER 8/25/03